

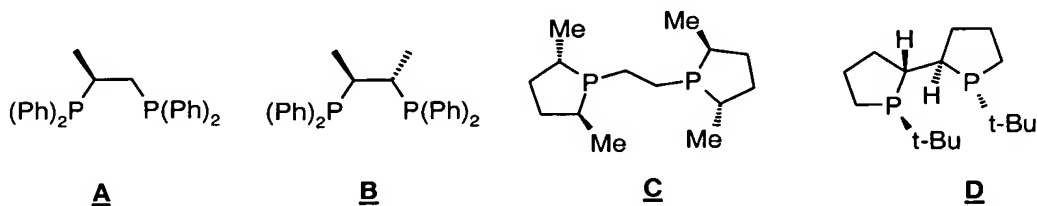
PHOSPHINE LIGANDS

Field of the Invention

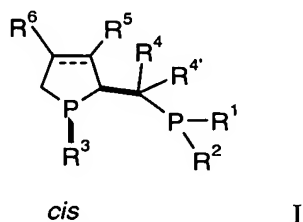
[0001] The present invention is related to new phosphine ligands, metal complexes of such ligands, as well as the use of such metal complexes as catalysts in asymmetric reactions.

Background of the Invention

[0002] Phosphine ligands with chiral centers on carbon and phosphorous atoms are known in the art. A particular class of phosphine ligands are those linked by a bridge of two carbon atoms, i.e., 1,2-diphosphine ligands. Examples of 1,2-diphosphine ligands with one or two chiral centers on the carbon atoms of the bridge are PROPHOS (A) as described in *J. Am. Chem. Soc.* 1978, 100, 5491; and CHIRAPHOS (B) see *J. Am. Chem. Soc.* 1977, 99, 6262. Another type of 1,2-diphosphine ligands are those where the chiral center is on C atoms in a phospholane ring such as for example in the BPE ligand (C), described in *Tetrahedron Asymmetry*, 1991, 2,(7), 569. Still another type of 1,2-diphosphine ligands are those where the chiral centers are on the C and P atoms such as in compound D, described in *Angew. Chem. Int. Ed.* 2002, 41(9), 1612.

Summary of the Invention

[0003] The present invention provides a new phosphine ligands of the formula I



wherein

R^1 and R^2 are independently of each other unsubstituted alkyl, aryl, cycloalkyl or heteroaryl, or alkyl, aryl, cycloalkyl or heteroaryl each of which independently is substituted by alkyl, alkoxy, halogen, hydroxy, amino, mono- or dialkylamino, aryl, $-SO_2-$, R^7 , $-SO_3^-$, $-CO-NR^8R^8$, carboxy, alkoxycarbonyl, trialkylsilyl, diarylalkylsilyl, dialkylarylsilyl or triarylsilyl;

R^3 is alkyl, cycloalkyl, aryl or heteroaryl;

$R^{4'}$ and R^4 are independently of each other hydrogen, alkyl, aryl or substituted aryl; or $R^{4'}$ and R^4 together, with the C-atom they are attached, form a 3-8-membered carbocyclic ring;

dotted line is optionally a double bond;

R^5 and R^6 are independently of each other hydrogen, alkyl or aryl;

R^7 is alkyl, aryl or NR^8R^8 ; and

R^8 and R^8 are independently of each other hydrogen, alkyl or aryl;

the substituents R^3 on the phospholane phosphorus atom and the substituent on the C2 atom of the phospholane ring being in *cis* relation to each other as indicated by the bold bonds in formula I.

[0004] The residues R^4 , $R^{4'}$, R^5 and R^6 may form additional chiral centers on the C atom they are attached to and the residues R^1 and R^2 may form an additional chiral center on the phosphorus atom they are attached to.

[0005] The present invention is also directed to chiral 1,2-diphosphine ligands with one chiral center on a carbon atom of the bridge and one chiral center on the phosphorous atom, i.e., a new bidentate C,P-chiral 1,2-diphosphine ligand system which form fairly rigid bicycle[3.3.0]octane chelates with transition metals.

Detailed Description of the Invention

[0006] The following definitions of the general terms used in the present description apply irrespective of whether the terms in question appear alone or in combination.

[0007] The term "alkyl" as used herein signifies straight-chain or branched hydrocarbon groups with 1 to 8 carbon atoms, preferably 1 to 6 carbon atoms, such as methyl, ethyl,

propyl, *iso*-propyl, butyl, *iso*-butyl and *tert.*-butyl. Preferably the alkyl groups for R¹, R² and R³ are branched alkyl groups such as *iso*-propyl, *iso*-butyl and *tert.*-butyl.

[0008] The term "alkoxy" denotes a group wherein the alkyl residue is as defined above, and which is attached via an oxygen atom.

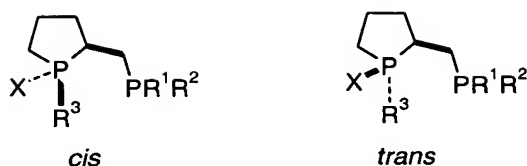
[0009] The term "cycloalkyl" stands for 3- to 8-membered rings, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, especially for cyclopentyl or cyclohexyl. Unless otherwise stated, said "alkyl" and "cycloalkyl" groups may be substituted by alkyl (for cycloalkyl), alkoxy, halogen, hydroxy, amino, mono- or dialkylamino, or aryl.

[0010] The term "aryl" signifies an aromatic hydrocarbon residue, especially the phenyl residue, which can be unsubstituted or substituted in the ortho-, meta- or para-position or multiply-substituted. Substituents which come into consideration are e.g. phenyl, alkyl or alkoxy groups, preferably methyl or methoxy groups, or amino, monoalkyl- or dialkylamino, preferably dimethylamino or diethylamino, or hydroxy, or halogen such as chlorine, or trialkylsilyl, such as trimethylsilyl. Moreover, the term "aryl" can signify naphthyl. Preferred aryl residues are phenyl, tolyl, dimethylphenyl, di-*tert.*-butylphenyl or anisyl.

[0011] The term "heteroaryl" signifies a 5- or 6-membered aromatic cycle containing one or more heteroatoms such as S, O and/or N. Examples of such heteroaryl groups are furyl, thienyl, benzofuranyl or benzothienyl.

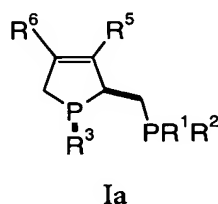
[0012] The compounds of the invention have two chiral centers, one on the P atom in the phospholane ring and one on the C2 atom of the phospholane ring. The substituents at these chiral centers are always in *cis* relation to each other.

[0013] For the denotation of *cis*- and *trans* configuration in the compounds of the invention and of related compounds the convention depicted below is adhered to:



X = lone pair, O, BH₃

[0014] Compound of formula Ia is an example of a compound of formula I, wherein R⁵ and R⁶ are independently of each other hydrogen, alkyl or aryl, and the dotted line is present and forms a double bond:



[0015] Preferred compounds of formula I are those wherein

R¹ and R² are the same and are unsubstituted alkyl, aryl, cycloalkyl or heteroaryl, or alkyl, aryl, cycloalkyl or heteroaryl each of which is independently substituted by alkyl, alkoxy, halogen, hydroxy, amino, mono- or dialkylamino, aryl, -SO₂-R⁷, -SO₃⁻, -CO-NR⁸R^{8'}, carboxy, alkoxycarbonyl, trialkylsilyl, diarylalkylsilyl, dialkylarylsilyl or triarylsilyl;

R³ is alkyl or aryl;

R^{4'} and R⁴ are hydrogen;

R⁵ and R⁶ are independently of each other hydrogen, C₁-C₃-alkyl or phenyl;

the dotted line is absent;

R⁷ is alkyl, aryl or NR⁸R^{8'}; and

R⁸ and R^{8'} are independently of each other hydrogen, alkyl or aryl;

the substituents R³ on the phospholane phosphorus atom and the substituent on the C2 atom of the phospholane ring being in *cis* relation to each other as indicated by the bold bonds in formula I.

[0016] One embodiment of the invention is compounds of formula I wherein

R¹ and R² are the same and are aryl;

R³ is *tert.*-butyl or phenyl;

R^{4'} and R⁴ are identical and signify hydrogen;
R⁵ and R⁶ are hydrogen; and the dotted line is absent.

[0017] Another embodiment is compounds of formula I wherein

R¹ and R² are the same and are alkyl;
R³ is *tert.*-butyl or phenyl;
R^{4'} and R⁴ are the same and are hydrogen;
R⁵ and R⁶ are hydrogen; and the dotted line is absent.

[0018] Another embodiment is compounds of formula I wherein

R¹ and R² are the same and are cycloalkyl;
R³ is *tert.*-butyl or phenyl;
R^{4'} and R⁴ are the same and are hydrogen;
R⁵ and R⁶ are hydrogen; and the dotted line is absent.

[0019] A further embodiment is compounds of formula I wherein

R¹ and R² are alike and signify heteroaryl;
R³ is *tert.*-butyl or phenyl;
R^{4'} and R⁴ are identical and signify hydrogen;
R⁵ and R⁶ are hydrogen; and the dotted line is absent.

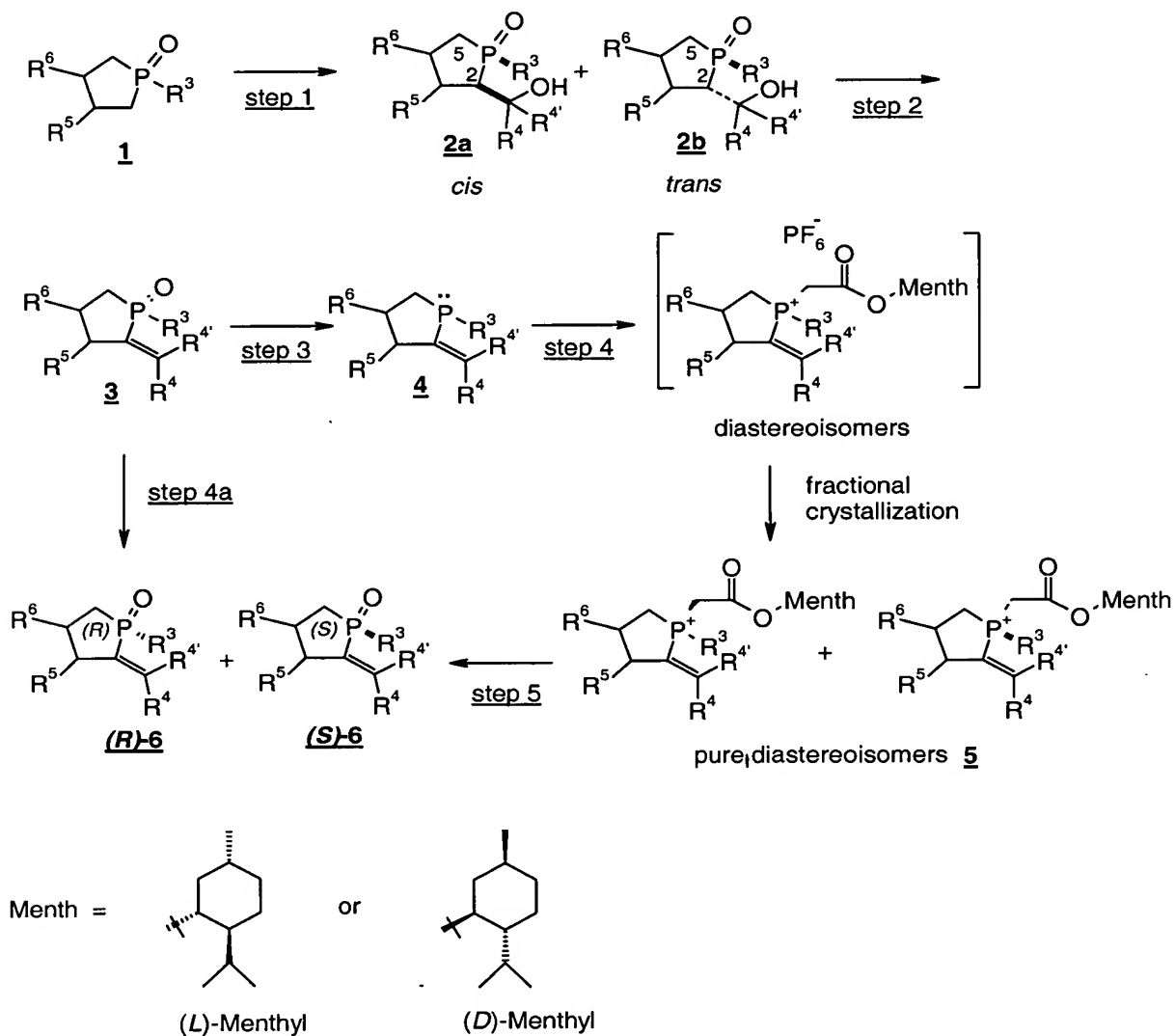
[0020] Especially preferred ligands of formula I are those wherein R¹ and R² are the same and are phenyl, R³ is phenyl and R⁴, R^{4'}, R⁵ and R⁶ are hydrogen.

[0021] The ligands of formula I are prepared according to the reaction scheme 1 to 3. The starting materials are known in the art and commercially available.

[0022] The synthesis of 2-methylenephospholane-1-oxide is carried out according to scheme 1 starting from the appropriately substituted phospholane-1-oxide (1) which may be prepared in analogy to the method described for 1-phenylphospholane-1-oxide in *J. Org. Chem.* 1971, 36, 3226.

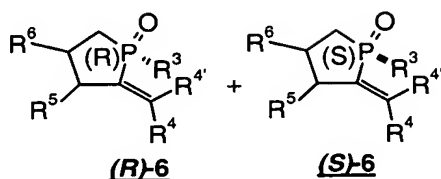
[0023] In the generic formulae of the schemes (R)- and (S)-configurational assignments of the phospholane phosphorus atom are based on the Cahn-Ingold-Prelog rules with an arbitrarily chosen priority of $R^3 > C2$ of phospholane ring $> C5$ of phospholane ring.

Scheme 1



wherein the residues are as defined above for formula I.

[0024] The optical active intermediates of formula 6



wherein R^3 , R^4 , R^4' , R^5 and R^6 are as defined for formula I above;
are new and thus part of the present invention.

Step 1

[0025] The phospholane 1-oxide (1) is metallated with a metallation reagent, such as an aryl or alkyl lithium reagent or a lithium amide reagent and subsequently reacted with an aldehyde such as e.g., formaldehyde or a ketone such as e.g., acetone to yield mixtures of *cis*- and *trans*-2-phospholanemethanol 1-oxide (2a and 2b). Metallation reagents may be phenyl-, butyl-, *sec*- and *tert*-butyllithium or the like, or lithium-di-*iso*-propylamide, lithium-2,2,6,6-tetramethylpiperidide or the like. In a preferred version an aryl or alkyl lithium reagent is used which contains the aryl or alkyl group R^3 .

Step 2

[0026] 2-Methylene-oxo-phospholane (3) is formed by dehydration of *cis*- or *trans* 2-phospholanemethanol 1-oxide (2a and b) or of mixtures thereof. Such dehydration can be performed by methods known to the person skilled in the art. For example, the dehydration can be performed by reaction of the hydroxy group with an inorganic acid chloride such as thionylchloride or phosphoroxichloride and subsequent elimination of the formed chloride intermediate, for example, in presence of an organic base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO), triethylamine or pyridine or the like. In another method the dehydration is performed by catalysis with a strong acid such as e.g., sulfuric acid, phosphoric acid, pyrophosphoric acid, potassium hydrogen sulfate, *p*-toluenesulfonic acid, etc. In still another method an ester derived from an organic acid such as methanesulfonic acid or *p*-toluenesulfonic acid is formed and the subsequent elimination performed with an organic base such as 1,8-diazabicyclo[5.4.0]undec-7-ene, triethylamine or pyridine or the like. In yet another method, an ester derived from acetic acid is formed and subjected to pyrolytic elimination.

Step 3

[0027] 2-Methylenephospholane-1-oxide (3) is reduced to the corresponding phospholane (4) by methods known in the art. Such reduction can be achieved, for example, by treatment with silane reagents (e.g., trichlorosilane, hexachlorodisilane, phenylsilane, polymethylhydrosiloxane, etc.), aluminum reagents (e.g., lithium or sodium aluminum hydride, aluminum hydride), metals (aluminum, magnesium) or with hydrogen after activation with phosgene.

Steps 4 and 5

[0028] On the one hand optical resolution of 2-methylenephospholane (4) by quaternisation reaction with an optically active alkylating agent such as, for example, with (*L*)- or (*D*)-methyl-2-bromo-acetate and fractional crystallization of the salt yields the diastereomerically pure methyl acetate derivatives (5), which then are cleaved in the presence of a base such as sodium hydroxide to the enantiomerically pure 2-methylene-1-oxo-phospholanes (6).

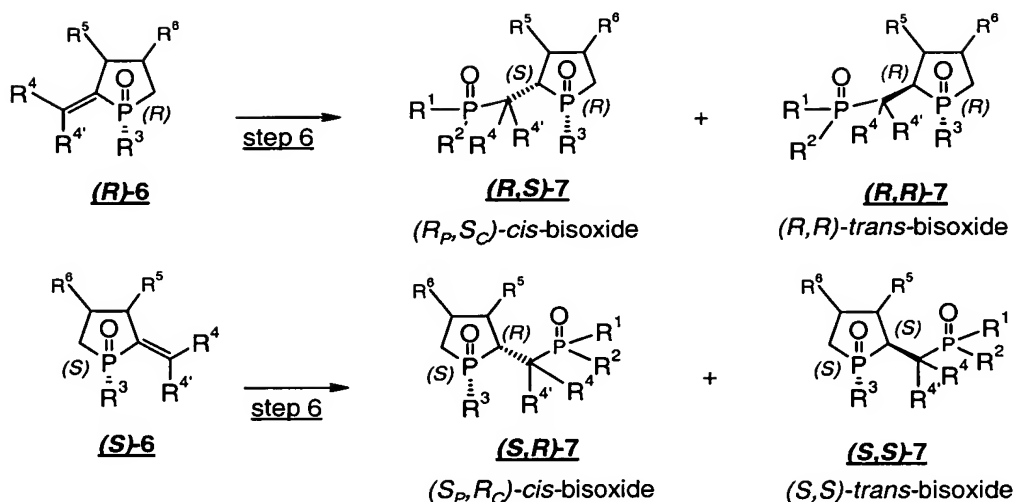
Step 4a

[0029] On the other hand 2-methylene-1-oxo-phospholane (3) can be separated into the enantiomerically pure 2-methylene-1-oxo-phospholanes (6) by chromatography on a chiral support.

Step 6

[0030] The enantiomerically pure 2-methylenephospholane-1-oxides (6) are transformed into a mixture of the corresponding *cis*- and *trans*-bisoxides (7) according to scheme 2.

Scheme 2



wherein the residues are as defined above for formula I.

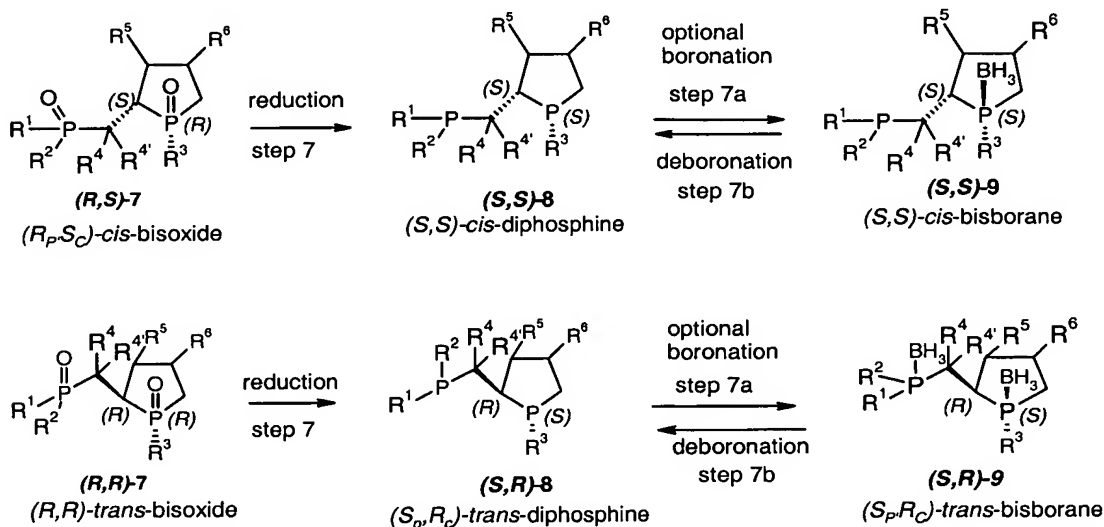
[0031] The transformation is performed by adding a secondary phosphine oxide which can proceed under purely thermal conditions by heating or under base catalysis conditions, e.g., with amine bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) or sodium hydride, sodium ethoxide or the like. Alternatively the transformation can also be performed step-wise by addition of a secondary phosphine in the presence of a base such as e.g., potassium *tert*-butoxide or by addition of a preformed secondary lithium phosphide to yield the phosphine addition product and subsequent oxidation with hydrogen peroxide.

Step 7

[0032] The bisoxides (7) are reduced to the diphosphines (8) which optionally can be purified and stored as bis(borane) adducts (9) and which from the diphosphines can be regenerated by deboration as depicted in scheme 3:

Scheme 3

(drawn for diastereoisomers (S,S)-8 and (S,R)-8; the diastereoisomers (R,R)-8 and (R,S)-8 can be prepared analogously from (S,R)-7 and (S,S)-7)



wherein the symbols are as defined above for formula I.

[0033] These methods are standard methods and known to the person skilled in the art. The reduction (step 7) can be achieved, for example, by treatment with silane reagents (e.g., trichlorosilane, hexachlorodisilane, phenylsilane, and polymethylhydrosiloxane), or with aluminum reagents (e.g., lithium or sodium aluminum hydride, and aluminum hydride). The boronation (step 7a) can be performed, for example, by treatment of the diphosphines with a borane-delivering agent such as e.g., the borane-tetrahydrofuran complex, the borane-N,N-diethylaniline complex, the borane-dimethylsulfide complex or the like. Alternatively, the reduction and boronation (steps 7 and 7a) can also be performed as a single protocol, e.g., by treatment of the bisoxides with lithium aluminum hydride in the presence of sodium borohydride and cerium trichloride, to provide directly the bis(borane) adducts. The bis(borane) adducts may be purified by chromatography or crystallization to achieve high chemical purity. The deboronation (step 7b) can be achieved by treatment of the bis(borane) adducts with an amine base such as e.g., 1,4-diazabicyclo[2.2.2]octane (DABCO), pyrrolidine, diethylamine or the like or by treatment with an acid such as HBF₄ or the like.

[0034] The optically active ligands of formula I form complexes with transition metals, especially with transition metals of Group VIII, such as ruthenium, rhodium, iridium,

palladium and nickel. These complexes can be used as catalysts in asymmetric reactions such as hydrogenations and enantioselective hydrogen displacements in prochiral allylic systems. Preferably, the metal complexes are used in their isolated forms for the hydrogenations. Alternatively, the complexes may be prepared *in situ*.

[0035] These catalysts, i.e., the complexes of a transition metal and the chiral diphosphine ligands of formula I, are novel and are likewise an aspect of the present invention.

[0036] The aforementioned transition metal complexes, especially the complexes with metals of group VIII can be represented by the following formula II and III indicated below:



wherein

M is a transition metal,
 L is the diphosphine compound of formula I;
 X is a coordinating anion, such as Cl, Br or I
 m, n and p are each 1, and
 q is 0, if M is Rh;

or

X is acyloxy, such as acetoxy, trifluoroacetoxy or pivaloyloxy,
 m and n are each 1,
 p is 2, and
 q is 0, if M is Ru;

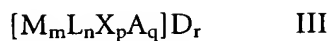
or

X is Cl,
 m and n are each 2,
 p is 4,
 q is 1, and
 A is triethylamine, if M is Ru;

or

X is a π -methallyl group,
 m and n are each 1,
 p is 2, and
 q is 0, if M is Ru;

or
 X is a coordinating anion, such as Cl, Br or I,
 m, n and p are each 1, and
 q is 0, if M is Ir;
 or
 X is Cl,
 m and n are each 1,
 p is 2, and
 q is 0, if M is Pd;
 or
 X is Cl, Br or I,
 m and n are each 1,
 p is 2, and
 q is 0, if M is Ni.



wherein

M is a transition metal,
 L is the diphosphine compound of formula I,
 X is a diene ligand, such as cod or nbd (both as defined below),
 D is a non-coordinating anion, such as BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF (as defined below),
 m, n, p and r are each 1, and
 q is 0, if M is Rh;
 or
 X is an olefinic ligand, such as cyclooctene or ethylene,
 D is a non-coordinating anion, such as BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF,
 m, n and r are each 1,
 p is 2 and
 q is 0, if M is Rh;
 or
 X is Cl, Br or I,
 A is benzene or p-cymene,

D is Cl, Br or I, and
 m, n, p, q and r are each 1, if M is Ru;
 or
 D is a non-coordinating anion, such as BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF,
 m and n are each 1,
 p and q are each 0, and
 r is 2, if M is Ru;
 or
 X is a diene ligand, such as cod or nbd,
 D is a non-coordinating anion, such as e.g., BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF,
 m, n, p and r are each 1, and
 q is 0, if M is Ir;
 or
 X is an olefinic ligand, such as e.g., cyclooctene or ethylene,
 D is a non-coordinating anion, such as e.g., BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF,
 m, p and r are each 1,
 n is 2, and
 q is 0, if M is Ir;
 or
 X is a π -allyl group,
 D is a non-coordinating anion, such as e.g., BF₄, ClO₄, PF₆, SbF₆, CF₃SO₃, BPh₄, or BARF,
 m, n, p and r are each 1, and
 q is 0, if M is Pd.

[0037] Ph is a phenyl group, cod is (Z,Z)-1,5-cyclooctadiene, nbd is norbornadiene, and BARF is tetrakis[3,5-bis(trifluoromethyl)phenyl]borate. π -Methallyl and π -allyl is anionic ligands of the structures H₂C=C(Me)-CH₂ and H₂C=CH-CH₂.

[0038] Preferred transition metal complexes and methods for making such complexes are described below.

[0039] A ruthenium complex can be prepared, for example, by reaction of the Ru precursors $[\text{Ru}(\text{cod})(\text{OCOCF}_3)_2]_2$, $[\text{Ru}(\text{cod})(\text{OCOCF}_3)_2]_2 \cdot \text{H}_2\text{O}$, $[\text{Ru}(\text{cod})(\text{OCOCH}_3)_2]$ or $[\text{Ru}_2(\text{cod})_2\text{Cl}_4(\text{CH}_3\text{CN})]$ and the ligand of formula I in an inert solvent, for example, in ethers such as tetrahydrofuran or diethyl ether or mixtures thereof, or in dichloromethane as described in the literature (B. Heiser, E.A. Broger, Y. Crameri, *Tetrahedron: Asymmetry* 1991, 2, 51). Another method for preparing a ruthenium complex comprises, for example, the reaction of the ruthenium precursor $[\text{Ru}(\text{cod})(\text{methallyl})_2]$ with a ligand of the formula I in a nonpolar solvent such as e.g., hexane or toluene or mixtures thereof as described in J.P. Genet, S. Mallart, C. Pinel, S. Juge, J.A. Laffitte, *Tetrahedron: Asymmetry*, 1991, 2, 43.

[0040] *In situ* preparation of ruthenium complexes can be performed, for example, by reaction of the ruthenium precursor $[\text{Ru}(\text{cod})(\text{methallyl})_2]$ with a ligand of the formula I in the presence of trifluoroacetic acid in methanol as described in the literature (B. Heiser, E.A. Broger, Y. Crameri, *Tetrahedron: Asymmetry* 1991, 2, 51).

[0041] A ruthenium complex can also be prepared, for example, by heating $[\text{Ru}(\text{cod})\text{Cl}_2]_n$ and the ligand of formula I at reflux by use of toluene as a solvent in the presence of triethylamine as described in the literature (T. Ikariya, Y. Ishii, H. Kawano, T. Arai, M. Saburi, and S. Akutagawa, *J. Chem. Soc., Chem. Commun.* 1985, 922). Further, a ruthenium complex can be prepared, for example, by heating $[\text{Ru}(\text{p-cymene})\text{I}_2]_2$ and the ligand of formula I with stirring in a methylene chloride/ethanol mixture in accordance with the method described in the literature (K. Mashima, K. Kusano, T. Ohta, R. Noyori, H. Takaya, *J. Chem. Soc., Chem. Commun.* 1989, 1208).

[0042] Preferred ruthenium complexes are $\text{Ru}(\text{OAc})_2(\text{L})$, $[\text{Ru}(\text{OCOCF}_3)_2(\text{L})]_2$, $\text{Ru}_2\text{Cl}_4(\text{L})_2 \cdot \text{NEt}_3$, $[\text{RuCl}(\text{benzene})(\text{L})]\text{Cl}$, $[\text{RuBr}(\text{benzene})(\text{L})]\text{Br}$, $[\text{RuI}(\text{benzene})(\text{L})]\text{I}$, $[\text{RuCl}(\text{p-cymene})(\text{L})]\text{Cl}$, $[\text{RuBr}(\text{p-cymene})(\text{L})]\text{Br}$, $[\text{RuI}(\text{p-cymene})(\text{L})]\text{I}$, $[\text{Ru}(\text{L})](\text{BF}_4)_2$, $[\text{Ru}(\text{L})](\text{ClO}_4)_2$, $[\text{Ru}(\text{L})](\text{PF}_6)_2$ and $[\text{Ru}(\text{L})](\text{BPh}_4)_2$.

[0043] A rhodium complex can be prepared, for example, by reaction of rhodium precursors such as $[\text{Rh}(\text{cod})\text{Cl}]_2$, $[\text{Rh}(\text{nbd})\text{Cl}]_2$, $[\text{Rh}(\text{cod})_2]\text{SbF}_6$, $[\text{Rh}(\text{cod})_2]\text{BF}_4$, $[\text{Rh}(\text{cod})_2]\text{ClO}_4$ with the ligand of formula I in accordance with the method described in "Experimental Chemistry, 4th edition" Vol.18, Organometallic Complexes, pp.339-344, Ed. Chemical Society of Japan, 1991, Maruzen.

[0044] Preferred rhodium complexes are

$\text{Rh}(\text{L})\text{Cl}$, $\text{Rh}(\text{L})\text{Br}$, $\text{Rh}(\text{L})\text{I}$, $[\text{Rh}(\text{cod})(\text{L})]\text{SbF}_6$, $[\text{Rh}(\text{cod})(\text{L})]\text{BF}_4$, $[\text{Rh}(\text{cod})(\text{L})]\text{ClO}_4$, $[\text{Rh}(\text{cod})(\text{L})]\text{PF}_6$, $[\text{Rh}(\text{cod})(\text{L})]\text{BPh}_4$, $[\text{Rh}(\text{cod})(\text{L})]\text{BARF}$, $[\text{Rh}(\text{nbd})(\text{L})]\text{SbF}_6$, $[\text{Rh}(\text{nbd})(\text{L})]\text{BF}_4$, $[\text{Rh}(\text{nbd})(\text{L})]\text{ClO}_4$, and $[\text{Rh}(\text{nbd})(\text{L})]\text{PF}_6$, $[\text{Rh}(\text{nbd})(\text{L})]\text{BPh}_4$.

[0045] An iridium complex can be prepared, for example, by reacting the ligand of formula I with $[\text{Ir}(\text{cod})(\text{CH}_3\text{CN})_2]\text{BF}_4$ or with $[\text{Ir}(\text{cod})\text{Cl}]_2$ in accordance with the method described in the literature (K. Mashima, T. Akutagawa, X. Zhang, H. Takaya, T. Taketomi, H. Kumobayashi, S. Akutagawa, J. Organomet., Chem. 1992, 428, 213).

[0046] Preferred iridium complexes are

$\text{Ir}(\text{L})\text{Cl}$, $\text{Ir}(\text{L})\text{Br}$, $\text{Ir}(\text{L})\text{I}$, $[\text{Ir}(\text{cod})(\text{L})]\text{BF}_4$, $[\text{Ir}(\text{cod})(\text{L})]\text{ClO}_4$, $[\text{Ir}(\text{cod})(\text{L})]\text{PF}_6$, $[\text{Ir}(\text{cod})(\text{L})]\text{BPh}_4$, $[\text{Ir}(\text{nbd})(\text{L})]\text{BF}_4$, $[\text{Ir}(\text{nbd})(\text{L})]\text{ClO}_4$, $[\text{Ir}(\text{nbd})(\text{L})]\text{PF}_6$, and $[\text{Ir}(\text{nbd})(\text{L})]\text{BPh}_4$

[0047] A palladium complex can be prepared, for example, by reaction of the ligand of formula I with π -allylpalladium chloride in accordance with the method described in a literature (Y. Uozumi and T. Hayashi, J. Am., Chem. Soc. 1991, 113, 9887).

[0048] Preferred palladium complexes are

$\text{PdCl}_2(\text{L})$, $[\text{Pd}(\pi\text{-allyl})(\text{L})]\text{BF}_4$, $[(\text{Pd}(\pi\text{-allyl})(\text{L}))]\text{ClO}_4$, $[(\text{Pd}(\pi\text{-allyl})(\text{L}))]\text{PF}_6$, and $[(\text{Pd}(\pi\text{-allyl})(\text{L}))]\text{BPh}_4$

[0049] A nickel complex can be prepared, for example, by dissolving the ligand of formula I and nickel chloride in an alcohol such as isopropanol or ethanol or mixtures thereof and heating the solution with stirring in accordance with the method described in "Experimental

Chemistry, 4th edition" Vol.18, Organometallic Complexes, pp.376, Ed. Chemical Society of Japan, 1991, Maruzen.

[0050] Preferred examples of nickel complexes are $\text{NiCl}_2(\text{L})$, $\text{NiBr}_2(\text{L})$ and $\text{NiI}_2(\text{L})$.

[0051] The transition metal complexes prepared as described above can be used as catalysts for asymmetric reactions, in particular for asymmetric hydrogenation reactions.

[0052] The following examples serve to illustrate the invention and do not in any manner represent a limitation.

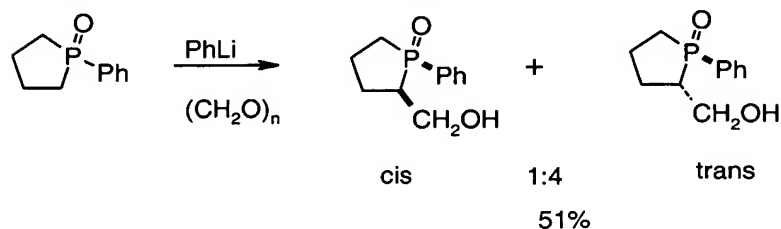
[0053] In the examples the selected abbreviations have the follow meanings:

h	hour
m.p.	melting point
THF	tetrahydrofuran
EtOAc	ethyl acetate
DBU	1,8-diazabicyclo(5,4,0)undec-7-ene
DABCO	1,4-diazabicyclo[2.2.2]octane
BARF	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
c	concentration
S/C	molar substrate catalyst ratio
conv.	conversion
ee	enantiomeric excess
GC	gaschromatography
PMP5	2-[(diphenylphosphino)methyl]-1-phenyl-phospholane
cod	(Z,Z)-1,5-cyclooctadiene

[0054] All experiments were carried out under an atmosphere of deoxygenated argon. Solvents were dried and distilled under argon before use. The metal diphosphine complexes were prepared using Schlenk techniques.

Example 1

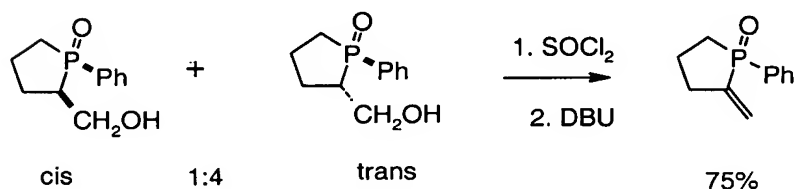
Preparation of 1-Phenyl-2-phospholanemethanol-1-oxide



[0055] In a 1 l round bottom 2-neck flask charged with a magnetic stirring bar, 23.4 g 1-phenylphospholane-1-oxide (0.11 mol) was dissolved in 300 ml freshly distilled THF, and 10.4 g dry paraformaldehyde was added. The reaction flask was flushed with argon and cooled to -20°C. Subsequently 100 ml phenyllithium solution in cyclohexane / diethylether 7 : 3 (1.8M) was added in one portion. The resulting mixture was stirred until the temperature reached +10°C and additionally 5 minutes at that temperature. Then 10 g NH₄Cl was added. The mixture was filtered, concentrated, and the residue purified by flash chromatography (EtOAc, followed by EtOAc/methanol 10:1). Yields: 2.5 g substrate (1-phenylphospholane-1-oxide) (11%), 11.7 g (43%) *trans*-1-phenyl-2-phospholanemethanol-1-oxide as white crystals, m.p. 109-110°C (toluene); ¹H NMR (500MHz) δ : 1.70-1.85 (m, 1H), 1.95-2.30 (m, 6H), 3.90-4.00 (m, 2H), 4.19 (t, 1H, *J* = 6.1), 7.45-7.55 (m, 3H), 7.70-7.76 (m, 2H); ³¹P NMR (200MHz) δ : 63.3; and 2.2 g (8%) *cis*-1-phenyl-2-phospholanemethanol-1-oxide, white crystals, m.p. 149-151°C (toluene); ¹H NMR (500MHz) δ : 1.46-1.57 (m, 1H), 2.02-2.22 (m, 4H), 2.28-2.42 (m, 1H), 2.44-2.58 (m, 1H), 3.32-3.49 (m, 2H), 3.76 (t, 1H, *J* = 5.7), 7.46-7.51 (m, 2H.), 7.52-7.57 (m, 1H), 7.67-7.73 (m, 2H); ³¹P NMR (200MHz) δ : 62.7.

Example 2

Preparation of 1-Phenyl-2-methylenephospholane-1-oxide

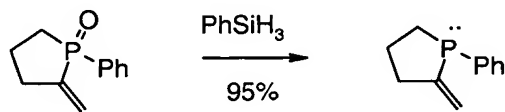


[0056] In a 100 ml round bottom 2-neck flask charged with a magnetic stirring bar and 20 ml freshly distilled CH_2Cl_2 , 1.6 g 1-phenyl-2-phospholanemethanol-1-oxide (0.008mol, mixture

of diastereoisomers) was dissolved. The reaction flask was flushed with argon and cooled to 0°C. Subsequently 2.1 ml SOCl₂ in 10 ml CH₂Cl₂ was added dropwise. The resulting yellowish mixture was stirred for 5h at room temperature, then 20 ml water was added. The mixture was extracted twice with 20ml CH₂Cl₂, and the combined organic phases were dried over MgSO₄ and filtered. To the resulting filtrate containing crude 2-chloromethyl-1-phenylphospholane 1-oxide (mixture of isomers; ³¹P NMR (200MHz) δ : 58.2, 60.3) 1.7 ml DBU was added. The mixture was heated and refluxed overnight. Evaporation of the solvent and flash chromatography of the residue with EtOAc/ethanol 20 :1 yielded 1.1g (75%) 1-phenyl-2-methylenephospholane-1-oxide as a colorless oil. ¹H NMR (500MHz) δ : 1.72-1.89 (m, 1H), 1.94-2.16 (m, 3H), 2.48-2.59 (m, 1H), 2.66-2.78 (m, 1H), 5.74 (dt, 1H, *J* = 2.4, *J* = 17.2), 5.88 (dt, 1H, *J* = 2.1, *J* = 36.6), 7.37-7.48 (m, 3H), 7.63-7.70 (m, 2H); ³¹P NMR (200MHz) δ : 45.0.

Example 3

Preparation of 1-Phenyl-2-methylenephospholane

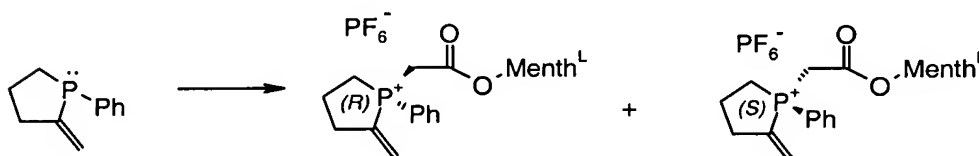


[0057] In a 250 ml round bottom 2-neck flask charged with a magnetic stirring bar and 60 ml freshly distilled toluene, 8.5 g 1-phenyl-2-methylenephospholane-1-oxide (0.04 mol) was dissolved and 11 g of PhSiH₃ was added. The flask was flushed with argon and the reaction mixture heated to 60°C for 2 days. Then the solvent was evaporated and the residue purified by flash chromatography (hexane followed by hexane/EtOAc 15:1) to yield 7.4g (95%) of 1-phenyl-2-methylenephospholane as a colorless oil, ¹H NMR (200MHz) δ : 1.55-2.10 (m, 4H), 2.20-2.65 (m, 2H), 5.51 (dd, 1H, *J* = 1.6, *J* = 11.0), 5.76 (dd, 1H, *J* = 1.5, *J* = 28.7), 7.05-7.50 (m, 5H), ³¹P NMR (200MHz) δ : -12.6.

Example 4a

Preparation of (1*R*)- and (1*S*)-1-Phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylene-phospholanium hexafluorophosphate

(alternative name {(1*R*)- and (1*S*)-1-Carboxymethyl-1-phenyl-2-methylenephospholanium hexafluorophosphate (*L*)-methyl ester})



[0058] In a 250 ml round bottom 1-neck flask charged with a magnetic stirring bar and 50 ml EtOAc, 7.4 g 1-phenyl-2-methylenephospholane (0.04mol) was dissolved and 12.8 g (*L*)-methyl bromoacetate was added. The mixture was stirred for 1.5 h; subsequently the solvent was evaporated. The oily residue was dissolved in 80 ml methanol and the solution was added dropwise to 7.5 g NH_4PF_6 dissolved in 40 ml water. The mixture turned turbid, and the formation of white oil was observed on the bottom. After standing overnight, white precipitate had formed. The precipitate was filtered and washed with water and 20 ml ethanol to afford 18.45 g of 1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate (1:1 mixture of diastereoisomers) as a white solid. This material was dissolved by heating it in 100 ml ethanol. The white crystals formed after standing overnight were collected. The procedure was repeated 5 times, until ^1H NMR showed diastereomeric purity.

[0059] Yield 5.02 g (24%) of diastereomerically pure (1*R*)-1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate as white crystals; m.p. 148.8-149.7°C (ethanol); $[\alpha]_D = +47.2$ ($c = 1.09$, CHCl_3); ^1H NMR (500MHz) δ : 0.56 (d, $J = 6.9$, 3H), 0.81 (d, $J = 7.0$, 3H), 0.88 (d, $J = 6.5$, 3H), 0.91-1.1 (m, 2H), 1.29-1.45 (m, 2H), 1.51-1.60 (m, 2H), 1.60-1.68 (m, 2H), 1.81-1.88 (m, 1H), 1.98-2.12 (m, 1H), 2.33-2.48 (m, 1H), 2.72-2.82 (m, 1H), 2.83-3.12 (m, 3H), 4.02 (dd, $J = 1.3$, $J = 13.7$, 2H), 4.64 (dt, $J = 4.4$, $J = 11.0$, 1H), 6.46 (d, $J = 18.9$, 1H), 6.55 (d, $J = 42.9$, 1H), 7.63-7.69 (m, 2H), 7.72-7.78 (m, 1H), 7.80-7.87 (m, 2H); ^{31}P NMR (500MHz) δ 31.3.

[0060] From the mother liquors fractional crystallization from methanol provided diastereomerically pure (1*S*)-1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate; m.p. 131.5-133°C (methanol); $[\alpha]_D = -116$ ($c = 1.03$, CHCl_3); ^1H NMR (500MHz) δ : 0.64 (d, $J = 6.9$, 3H), 0.82 (d, $J = 7.0$, 3H), 0.85 (d, $J = 6.5$, 3H), 0.87-1.2 (m, 2H), 1.29-1.43 (m, 2H), 1.60-1.70 (m, 2H), 1.70-1.77 (m, 1H), 2.01-2.14 (m, 1H), 2.32-2.46 (m, 1H), 2.75-3.08 (m, 4H), 3.99 (dq, $J = 13.7$, $J = 31.3$, 2H), 4.66 (dt, $J = 4.4$, $J = 11.0$, 1H), 6.42 (d, $J = 18.8$, 1H), 6.54 (d, $J = 42.8$, 1H), 7.63-7.69 (m, 2H), 7.72-7.78 (m, 1H), 7.80-7.88 (m, 2H); ^{31}P NMR (500MHz) δ 31.2.

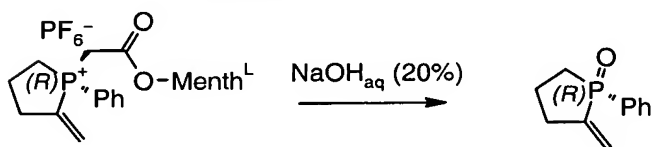
Example 4b

Preparation of (1*S*)-1-Phenyl-1-[2-[(*D*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate

[0061] In analogy to Example 4a, reaction of 1-phenyl-2-methylenephospholane with (*D*)-methyl bromoacetate provided diastereomerically pure (1*S*)-1-phenyl-1-[2-[(*D*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate; $[\alpha]_D = -44.3$ ($c = 1.15$, CHCl_3); NMR as above for (1*R*)-1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate (Example 4a).

Example 5a

Preparation of (*R*)-1-Phenyl-2-methylenephospholane-1-oxide



[0062] In a 250 ml round bottom 1-neck flask charged with a magnetic stirring bar and 50 ml CH_2Cl_2 , 9.16 g of (1*R*)-1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate was dissolved and 50 ml NaOH (20% aqueous solution) was added. The mixture was vigorously stirred for 2 h, then 100 ml water was added and the mixture extracted 3 times with 30 ml CH_2Cl_2 . The combined organic phases were dried over MgSO_4 , filtered and evaporated. The residue was purified by flash chromatography

with EtOAc/ethanol 20 :1 to yield 3.2 g (95%) of (*R*)-1-phenyl-2-methylenephospholane-1-oxide as a colorless oil; $[\alpha]_D = +107.9$ ($c = 2.21$, CHCl_3), NMR as above (Example 2).

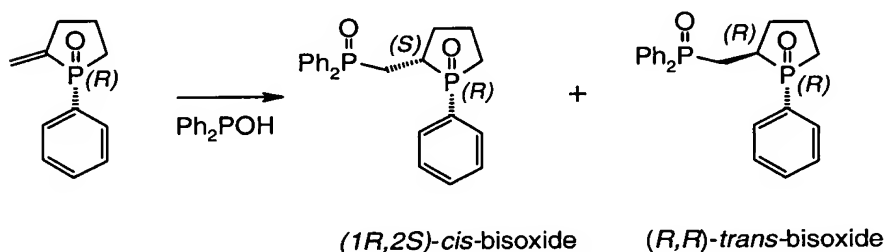
Example 5b

Preparation of (*S*)-1-Phenyl-2-methylenephospholane-1-oxide

[0063] Analogously, treatment of (*1S*)-1-phenyl-1-[2-[(*D*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate (or of (*1S*)-1-phenyl-1-[2-[(*L*)-methyloxy]-2-oxoethyl]-2-methylenephospholanium hexafluorophosphate) with NaOH (20%) provided (*S*)-1-phenyl-2-methylenephospholane-1-oxide as a colorless oil; NMR as above (Example 2).

Example 6

Preparation of (*1R,2S*)-*cis*-1-Phenyl-2-[(diphenylphosphinoyl)methyl]phospholane-1-oxide {(*1R,2S*)-*cis*-bis-oxide}

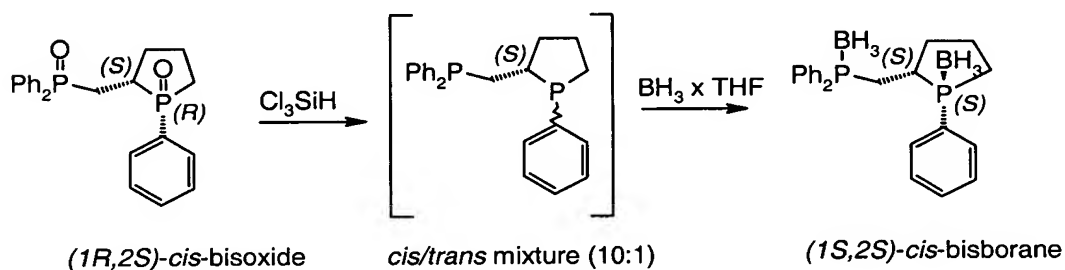


[0064] A 250 ml round bottom 2-neck flask equipped with a magnetic stirring bar was charged with a solution of 3.8 g of (*R*)-1-phenyl-2-methylenephospholane-1-oxide in 100 ml toluene. Then 4.35 g diphenylphosphine oxide was added to this solution. The mixture was heated under reflux overnight. The solvent was evaporated and the residue purified by flash chromatography with EtOAc/methanol 10:1 to yield 2.35 g (30%) of (*1R,2R*)-*trans*-1-phenyl-2-[(diphenylphosphinoyl)methyl]-phospholane-1-oxide {*R,R*-*trans*-bisoxide} as a colorless oil ^1H NMR (500MHz) δ : 1.60-1.74 (m, 2H), 1.93-2.06 (m, 1H), 2.09-2.46 (m, 4H), 2.49-2.57 (m, 1H), 2.75-2.86 (m, 1H), 7.28-7.34 (m, 2H), 7.38-7.53 (m, 7H), 7.56-7.66(m, 4H), 7.73-7.80 (m, 2H); ^{31}P NMR (200MHz) δ : 31.8 (d, $J = 42.4$), 59.1 (d, $J = 42.4$); $[\alpha]_D = +77.1$ ($c = 1.16$, CHCl_3); and 2.92g (37%) of (*1R,2S*)-*cis*-1-phenyl-2-[(diphenylphosphinoyl)methyl]-phospholane-1-oxide {*1R,2S*-*cis*-bisoxide}, as white crystals, mp.176°C (toluene); ^1H NMR (500MHz) δ : 1.50-1.75 (m, 2H), 1.93-2.25 (m, 4H), 2.30-2.50 (m, 2H), 2.53-2.70 (m, 1H),

7.35-7.80 (m, 15H.), ^{31}P NMR (200MHz) δ : 33.1 (d, $J = 51.5$), 65.5 (d, $J = 51.5$). $[\alpha]_{\text{D}} = +98.6$ ($c = 1.01$, CHCl_3).

Example 7

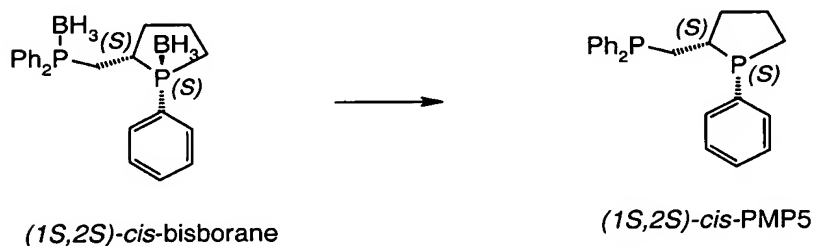
Preparation of (1*S*,2*S*)-cis-[1-Phenyl-2-[(diphenylphosphino)methyl]phospholane]bisborane
(alternative name {Hexahydro[μ -[(1*S*,2*S*)-[1-phenyl-2-[(diphenylphosphino- κ P)methyl]-phospholane- κ P]diboron})



[0065] A 250 ml round bottom 2-neck flask equipped with a magnetic stirring bar was flushed with argon and charged with 20 ml triethylamine and 80 ml dry toluene. Then 9 ml Cl_3SiH was added by syringe through a septum and 2.35g of (1*R*,2*S*)-cis-1-phenyl-2-[(diphenylphosphinoyl)methyl]phospholane-1-oxide dissolved in 50 ml dry toluene was added dropwise. The mixture was heated under reflux for 3.5 h. Subsequently 100 ml 20% aqueous NaOH was added and the mixture left overnight with stirring. The organic phase was separated and the water phase extracted twice with 80 ml toluene. The organic phases were collected, dried over Na_2SO_4 , filtered and evaporated. The residue was purified by flash chromatography on Al_2O_3 with hexane followed by hexane/EtOAc 20: 1. To the collected fractions containing the diphosphine 15 ml of a solution of BH_3 in THF (1M) was added. After 1 h the solvent was evaporated and the residue purified by flash chromatography with hexane/EtOAc 5 : 1 to yield 1.82 g (78%) of (1*S*,2*S*)-cis-[1-phenyl-2-[(diphenylphosphino)methyl]-phospholane]bisborane as white crystals, mp. 118-119°C (hexane : ethyl acetate); ^1H NMR (500MHz) δ : 0.35-1.35 (bt, 6H, $2 \times \text{BH}_3$), 1.35-1.50 (m, 1H), 1.50-1.63 (m, 1H), 1.70-1.85 (m, 1H), 2.15-2.55 (m, 6H) 7.3-7.8 (m, 15H, ar.).

Example 8a

Preparation of (1*S*,2*S*)-cis-1-Phenyl-2-[(diphenylphosphino)methyl]phospholane {(*S*,*S*)-cis-PMP5}



[0066] In a 100 ml round bottom 2-neck flask flushed with argon and equipped with a magnetic stirring bar, 155 mg DABCO was dissolved in 30 ml dry toluene. 270 mg of (*1S,2S*)-*cis*-[1-phenyl-2-[(diphenylphosphino)methyl]phospholane]bisborane was added and the mixture was stirred at 40°C overnight. The solvent was evaporated and the residue purified by flash chromatography on Al₂O₃ (hexane/EtOAc 20: 1) to afford 240 mg (96%) of (*1S,2S*)-*cis*-1-phenyl-2-[(diphenylphosphino)methyl]phospholane {(*S,S*)-*cis*-PMP5} as a turbid oil which solidified after standing for a few days yielding white powder, m.p. 74.5°C; ³¹P NMR (200MHz) δ : -16.3 (d, *J* = 26.6), -6.7 (d, *J* = 26.6); Elemental Anal. Calcd. for C₂₃H₂₄P₂: C 76.26%, H 6.68%, P 17.09%, found C 78.18%, H 6.62%, P 17. 20%.

Example 8b

Preparation of (1*R*,2*R*)-cis-1-Phenyl-2-[(diphenylphosphino)methyl]phospholane {(*R,R*)-cis-PMP5}

[0067] This ligand was prepared from (*S*)-1-phenyl-2-methylenephospholane-1-oxide analogously as described for (*S,S*)-*cis*-PMP5 in Examples 6-8a. (*1R,2R*)-*cis*-1-phenyl-2-[(diphenylphosphino)methyl]phospholane {(*R,R*)-*cis*-PMP5} turbid oil which solidified after standing for a few days; white powder, m.p. 74°C; [α]_D = -159.1 (*c* = 1.18, C₆H₆); ³¹P NMR as above.

Example 9

[0068] In the alternative approach the 1-phenyl-2-methylenephospholane-1-oxide (from example 2) can be separated into the enantiomerically pure 1-phenyl-2-methylenephospholane-1-oxide by chromatography on a chiral support.

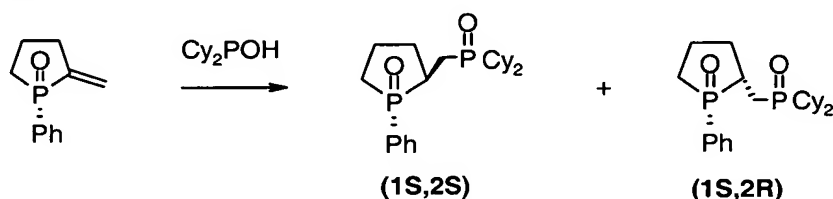
Resolution of 1-phenyl-2-methylenephospholane-1-oxide by preparative chromatography on a chiral support

[0069] Phenyl-2-methylenephospholane-1-oxide (3.0 g, chemical purity ca. 80%) was separated by repeated injections on a CHIRALPAK® AD 20 µm column (250 x 50 mm; mobile phase 100% acetonitrile, flow rate 120 ml/min) to afford 0.9 g of (*S*)-1-phenyl-2-methylenephospholane-1-oxide (ee 100%, chemical purity 95%; $[\alpha]_D = -99.6$ ($c = 1.03$, CHCl₃) and 1.0 g of (*R*)-1-phenyl-2-methylenephospholane-1-oxide (ee 99.4%, chemical purity 99.5%; $[\alpha]_D = +106.8$ ($c = 1.00$, CCHCl₃).

Example 10

Preparation of 2-(Dicyclohexyl-phosphinoylmethyl)-1-phenyl-phospholane 1-oxide

Step 1

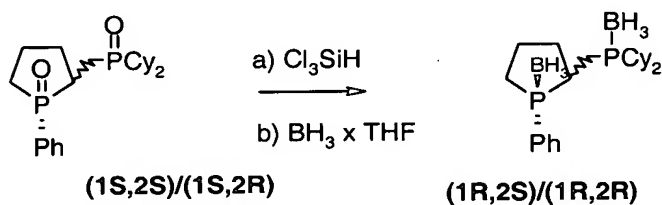


wherein Cy signifies cyclohexyl.

[0070] In a 250 ml round bottom 2-neck flask charged with a magnetic stirring bar 5.0 g (26 mmol) (*S*)-2-methylene-1-phenyl-phospholane 1-oxide and 5.6 g dicyclohexylphosphine oxide was dissolved in 100 ml dry THF. 1.2 g (2eq.) of potassium *tert*-butoxide was added and the reaction was stirred overnight. Next 500 ml of water was added and the mixture was extracted with chloroform (4 x 100 mL). Organic phase was dried over MgSO₄, concentrated and purified by chromatography (ethyl acetate: methanol 10:1). Yield: 4.99 g (47%) of (1*S*,2*S*)-2-[(dicyclohexylphosphinoyl)methyl]-1-phenyl-phospholane 1-oxide as white crystals, mp 110-114°C (ethyl acetate); ¹H NMR (500MHz) δ: 0.94-1.14 (m, 5H), 1.16-1.36 (m, 5H), 1.43-1.63 (m, 5H), 1.65-1.88 (m, 8H), 1.88-1.97 (m, 2H), 1.99-2.13 (m, 2H), 2.15-2.35 (m, 3H), 2.47-2.69 (m, 1H), 7.42-7.57 (m 3H), 7.63-7.74 (m, 2H); ¹³C NMR (126MHz) δ: 20.2 (d, $J = 58.7$), 23.4 (d, $J = 5.9$), 25.2-26.8 (m), 29.4 (d, $J = 66.9$), 33.9 (d, $J = 9.5$), 34.6 (dd, $J = 4.3$, $J = 67.2$), 36.8 (d, $J = 64.1$), 37.0 (d, $J = 64.2$), 128.7 (d, $J = 11.5$), 103.1 (d, $J = 9.6$), 131.9 (d, $J = 2.8$), 133.4 (d, $J = 88.3$); ³¹P NMR (162MHz) δ: 51.7 (d, $J = 34.8$), 59.3 (d, $J = 34.8$); EI MS m/z (%): 406 (2, M⁺), 324 (12), 323 (35), 242 (23), 241 (100), 193 (43), 179

(14), 146 (14), 55 (10); HR MS calcd. for $C_{23}H_{36}O_2P_2$: 406.2191, found 406.2185; $[\alpha]_D = -43.5^\circ$ ($c = 1.48$, $CHCl_3$); and 4.64 g (44%) of (1*S*,2*R*)-2-[(dicyclohexylphosphinoyl)methyl]-1-phenyl-phospholane 1-oxide as a white solid, mp 90-130°C (ethyl acetate); 1H NMR (500MHz) δ : 0.95-1.36 (m, 10H), 1.40-1.65 (m, 5H), 1.65-1.89 (m, 9H), 2.02-2.23 (m, 4H), 2.37-2.53 (m, 2H), 2.64-2.79 (m, 1H), 7.47-7.57 (m, 3H), 7.65-7.72 (m, 2H); ^{13}C NMR (126MHz) δ : 22.0 (d, $J = 57.6$), 22.3 (d, $J = 5.6$), 25.1-26.6 (m), 32.0 (d, $J = 12.6$), 36.3 (d, $J = 65.5$), 36.8 (d, $J = 64.1$), 37.2 (dd, $J = 5.0$, $J = 65.6$), 128.7 (d, $J = 11.1$), 130.9 (d, $J = 8.8$), 131.3 (d, $J = 87.7$), 132.0 (d, $J = 2.7$); ^{31}P NMR (162MHz) δ : 51.0 (d, $J = 41.4$), 64.3 (d, $J = 41.4$); EI MS m/z (%): 406 (1, M^{+}), 241 (100), 193 (57), 179 (19), 146 (22), 55 (18), 41 (16); HR MS calcd. for $C_{23}H_{36}O_2P_2$: 406.2191, found 406.2182; $[\alpha]_D = -36.4^\circ$ ($c = 1.67$, $CHCl_3$).

Step 2



[0071] The same procedure as for transformation of diphenylphosphinoyl derivatives described in Example 2 was employed. Yield: 81 % of (1*R*,2*S*)-2-[(dicyclohexylphosphanyl)methyl]-1-phenyl-phospholane *P,P*-diborane as white crystals, mp 138.5°C (ethyl acetate); 1H NMR (500MHz) δ : -0.1-0.9 (b, 6H), 0.9-1.1 (m, 6H), 1.1-1.4 (m, 6H), 1.45-2.0 (m, 13H), 2.05-2.3 (m, 4H), 2.5-2.7 (m, 2H), 7.42-7.52 (m, 3H), 7.68-7.77 (m, 2H); ^{13}C NMR (126MHz) δ : 18.0 (dd, $J = 6.8$, $J = 29.9$), 25.7-26.8 (m), 32.0 (d, $J = 32.5$), 32.5 (d, $J = 31.9$), 36.0 (d, $J = 34.6$), 36.0 (d, $J = 7.35$), 128.9 (d, $J = 9.7$), 130.3 (d, $J = 45.6$), 131.5 (d, $J = 2.6$), 131.7 (d, $J = 8.9$); ^{31}P NMR (202MHz) δ : 28.5 (b), 38.3 (b); LSIMS(+) MS m/z : 425 (5, $M + Na^+$), 402 (25), 275 (75); Elemental Anal. Calcd. for $C_{23}H_{42}B_2P_2$: C 68.69, H 10.53, found C 68.53, H 10.69; $[\alpha]_D = -76.2^\circ$ ($c = 0.80$, $CHCl_3$).

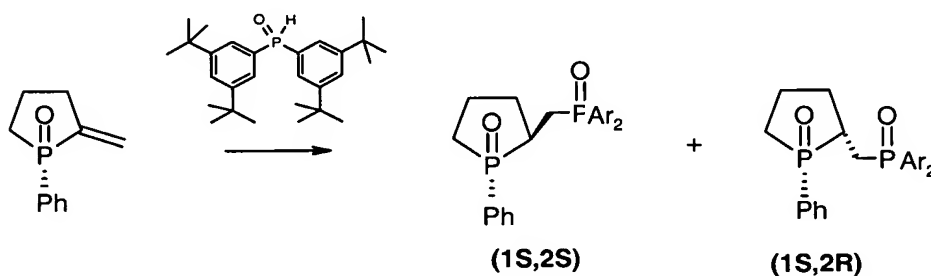
[0072] Using the same procedure but with the (1*S*,2*R*) derivative as a substrate yielded 84% of (1*R*,2*R*)-2-[(dicyclohexylphosphanyl)methyl]-1-phenyl-phospholane *P,P*-diborane as white crystals, mp 113.5-115°C (ethyl acetate); 1H NMR (500MHz) δ : -0.1-0.8 (b, 4H), 0.8-1.15 (m, 5H), 1.17-1.34 (m, 6H), 1.35-1.63 (m, 4H), 1.65-2.01 (m, 12H), 2.03-2.35 (m, 4H),

2.41-2.61 (m, 2H), 7.43-7.53 (m, 3H), 7.63-7.76 (m, 2H); ^{13}C NMR (126MHz) δ : 15.7 (d, $J = 1.7$), 23.5 (dd, $J = 8.5$, $J = 36.6$), 25.9-28.4 (m), 31.5 (d, $J = 28.8$), 32.3 (d, $J = 29.7$), 35.5 (d, $J = 33.1$), 39.6 (dd, $J = 1.4$, $J = 24.1$), 126.4 (d, $J = 44.4$), 128.8 (d, $J = 9.6$), 131.8 (d, $J = 2.4$), 133.0 (d, $J = 8.8$); ^{31}P NMR (202MHz) δ : 30.8 (b), 40.4 (b); LSIMS(+) MS m/z : 425 (14, $(\text{M} + \text{Na})^+$) 401 (100), 387 (66), 375 (47); Elemental Anal. Calcd. for $\text{C}_{23}\text{H}_{42}\text{B}_2\text{P}_2$: C 68.69, H 10.53, found C 68.47, H 10.36; $[\alpha]_{\text{D}} = -15.6^\circ$ ($c = 0.77$, CHCl_3).

Example 11

Preparation of 2-[Bis-(3,5-di-tert-butyl-phenyl)-phosphinoylmethyl]-1-phenyl-phospholane 1-oxide

Step 1



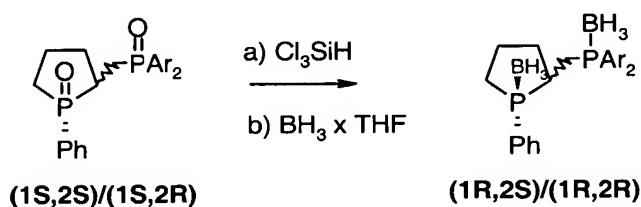
wherein Ar is di-*tert*-butyl-phenyl

[0073] The same procedure as for synthesis of diphenylphosphinoyl derivatives described in Example 6 was employed. Yield: 11% of (1S,2S)-2-[di(3,5-(di-*tert*-butyl-phenyl))phosphinoylmethyl]-1-phenyl-phospholane 1-oxide as white powder;

mp 149-150°C (hexane); ^1H NMR (500MHz) δ : 1.22 (s, 18H), 1.30 (s, 18H), 1.56-1.82 (m, 2H), 1.91-2.06 (m, 1H), 2.08-2.23 (m, 2H), 2.24-2.54 (m, 3H), 2.63-2.73 (m, 1H), 7.36-7.43 (m, 2H), 7.44-7.52 (m, 4H), 7.53-7.62 (m, 5H); ^{13}C NMR (126MHz) δ : 23.5 (d, $J = 6.4$), 28.2 (dd, $J = 2.3$, $J = 69.5$), 29.4 (d, $J = 66.8$), 31.2 (i), 31.3 (i), 32.3 (dd, $J = 1.5$, $J = 9.6$), 34.2 (dd, $J = 3.9$, $J = 66.7$), 34.9, 35.0, 124.7 (d, $J = 3.4$), 124.8 (d, $J = 3.7$), 125.8 (d, $J = 2.6$), 125.9 (d, $J = 2.7$), 128.7 (d, $J = 11.5$), 129.9 (d, $J = 9.6$), 131.6 (d, $J = 98.3$), 131.7 (d, $J = 2.8$), 132.8 (d, $J = 97.0$), 133.1 (d, $J = 88.5$), 151.1 (d, $J = 11.5$); ^{31}P NMR (202MHz) δ : 34.9 (d, $J = 43.8$), 60.4 (d, $J = 43.8$); EI MS m/z (%): 619 (19), 618 (47, M^+), 617 (12), 603 (10), 590 (26), 589 (56), 577 (37), 576 (100), 575 (56), 549 (11), 541 (20), 472 (10), 441 (22), 440 (31), 430 (27), 429 (99), 426 (14), 425 (24), 409 (13), 193 (37), 57 (36), 41 (10); Elemental Anal. Calcd. for $\text{C}_{39}\text{H}_{56}\text{O}_2\text{P}_2$:

C 75.70, H 9.12, found C 75.32, H 9.47; $[\alpha]_D = -56.3^\circ$ ($c = 0.95$, CHCl_3); and 83% of (1*S*,2*R*)-2-[di(3,5-(di-*tert*-butyl-phenyl))phosphinoyl)methyl]-1-phenyl-phospholane 1-oxide as white powder, mp 198-199°C (hexane/ethyl acetate); ^1H NMR (500MHz) δ : 1.26 (s, 18H), 1.30 (s, 18H), 1.47-1.69 (m, 2H), 1.92-2.21 (m, 5H), 2.29-2.60 (m, 2H), 7.41 (dd, $J = 1.8$, $J = 12.0$, 2H), 7.46 (dd, $J = 1.8$, $J = 12.2$, 2H), 7.49-7.59 (m, 5H), 7.69-7.75 (m, 2H); ^{13}C NMR (126MHz) δ : 22.5 (d, $J = 5.8$), 25.8 (d, $J = 66.7$), 29.5 (d, $J = 69.0$), 31.1 (d, $J = 12.3$), 31.2 (i), 31.3 (i), 35.0, 34.98, 35.01, 37.0 (dd, $J = 4.5$, $J = 65.6$), 124.8 (d, $J = 9.7$), 125.0 (d, $J = 10.0$), 125.8 (d, $J = 2.6$), 126.1 (d, $J = 2.6$), 128.7 (d, $J = 11.2$), 130.9 (d, $J = 98.2$), 130.9 (d, $J = 8.8$), 131.4 (d, $J = 86.8$), 132.0 (d, $J = 2.8$), 132.2 (d, $J = 99.4$), 151.1 (d, $J = 11.3$), 151.2 (d, $J = 11.4$); ^{31}P NMR (202MHz) δ : 34.9 (d, $J = 50.8$), 65.2 (d, $J = 50.8$); EI MS m/z (%): 619 (28), 618 (69, M^+), 603 (13), 591 (10), 590 (38), 589 (79), 577 (36), 576 (100), 575 (52), 549 (13), 472 (16), 442 (18), 441 (70), 440 (100), 439 (18), 426 (25), 425 (47), 409 (19), 398 (17), 384 (16), 294 (12), 193 (56), 57 (42), 41 (11); HR MS calcd. for $\text{C}_{39}\text{H}_{56}\text{O}_2\text{P}_2$: 618.3756, found 618.3736; $[\alpha]_D = -46.6^\circ$ ($c = 0.99$, CHCl_3).

Step 2



[0074] The same procedure as for transformation of diphenylphosphinoyl derivatives was employed as described in Example 7. Yield 81% of (1*R*,2*S*)-2-[di(3,5-(di-*tert*-butyl-phenyl))-phosphanyl)methyl]-1-phenyl-phospholane *P,P*-diborane; ^{31}P NMR (202MHz) δ : 17.4 (b), 39.9 (b).

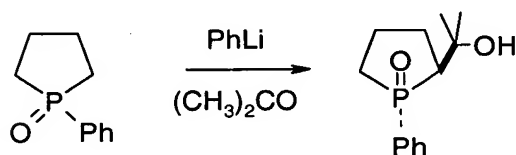
[0075] Using the same procedure but the (1*S*,2*R*) derivative as a substrate yielded 79 % of (1*R*,2*R*)-2-[di(3,5-(di-*tert*-butyl-phenyl))phosphanyl)methyl]-1-phenyl-phospholane *P,P*-diborane; ^1H NMR (500MHz) δ : 0.25-0.92 (b, 6H), 1.16 (s, 18H), 1.23 (s, 18H), 1.27-1.42 (m, 2H), 1.43-1.53 (m, 1H), 1.60-1.74 (m, 1H), 2.03-2.37 (m, 5H), 7.25 (dd, $J = 1.7$, $J = 11.2$, 2H), 7.36-7.49 (m, 7H), 7.58-7.67 (m, 2H); ^{13}C NMR (126MHz) δ : 23.6 (d, $J = 36.0$), 25.2, 26.8 (d, $J = 34.2$), 31.2 (i), 31.3 (i), 33.5, 35.0, 35.1, 35.9 (d, $J = 32.9$), 125.1 (d, $J = 2.3$), 125.7 (d, $J =$

2.3), 125.9 (d, $J = 9.7$), 126.4 (d, $J = 9.8$), 126.9 (d, $J = 54.2$), 127.6 (d, $J = 42.6$), 128.8 (d, $J = 9.2$), 129.3 (d, $J = 54.6$), 131.7 (d, $J = 2.4$), 132.9 (d, $J = 8.4$), 151.1 (d, $J = 9.6$), 151.4 (d, $J = 9.7$); ^{31}P NMR (202MHz) δ : 17.6 (b), 40.2 (b); LSIMS(+) MS m/z : 637 (17, $\text{M} + \text{Na}^+$), 614 (43, M^+), 611 (100), 599 (84), 587 (60).

Example 12

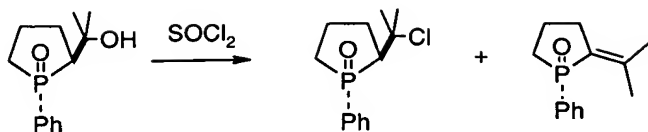
Synthesis of 2-(1-diphenylphosphino-1-methyl-ethyl)-1-phenylphospholane 1-oxide

Step 1



[0076] A 500 mL round bottom 2-neck flask equipped with a magnetic stirring bar was charged with 7.2 g of 1-phenylphospholane-1-oxide (40 mmol) dissolved in 200 mL of THF and cooled to -78°C (dry ice/acetone bath). Subsequently 40 mL (1.3 eq.) of phenyllithium solution in cyclohexane : diethyl ether 7:3 (1.3M) was added in one portion. The resulting dark solution was stirred 10 minutes and 2 mL of dry acetone was added. The mixture was stirred 10 minutes and additional 6 mL of acetone was added. After 5 minutes water (10 g) and NH_4Cl (10 g) was added. The mixture was filtered, concentrated, and the residue was purified by flash chromatography (ethyl acetate). Yield: 0.3 g of unreacted substrate 1-phenylphospholane-1-oxide (4%) and 8.2 g (86%) of trans-2-(1-hydroxy-1-methyl-ethyl)-1-phenylphospholane 1-oxide as white crystals; mp $112\text{--}114^\circ\text{C}$ (ethyl acetate); ^1H NMR (500MHz) δ : 1.17 (s, 3H), 1.27 (s, 3H), 1.53-1.68 (m, 1H), 1.85-1.93 (m, 1H), 1.95-2.33 (m, 5H), 4.5 (b, 1H), 7.38-7.52 (m, 3H), 7.62-7.70 (m, 2H); ^{13}C NMR (126MHz) δ : 23.2 (d, $J = 6.1$), 27.0 (d, $J = 11.3$), 29.1 (d, $J = 9.0$), 30.6 (d, $J = 2.8$), 31.4 (d, $J = 66.8$), 50.6 (d, $J = 66.5$), 71.6 (d, $J = 3.9$), 128.8 (d, $J = 11.6$), 129.8 (d, $J = 9.8$), 131.8 (d, $J = 2.9$), 134.5 (d, $J = 87.7$); ^{31}P NMR (81MHz) δ : 61.2; EI MS m/z (%): 223 (61), 220 (14), 203 (23), 181 (11), 180 (100), 179 (29), 160 (14), 152 (57), 141 (12), 132 (22), 105 (19), 104 (35), 81 (12), 77 (15), 55 (13), 47 (21), 43 (13), 41 (13); Elemental Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_2\text{P}$: C 65.53, H 8.04, found C 65.10, H 8.20.

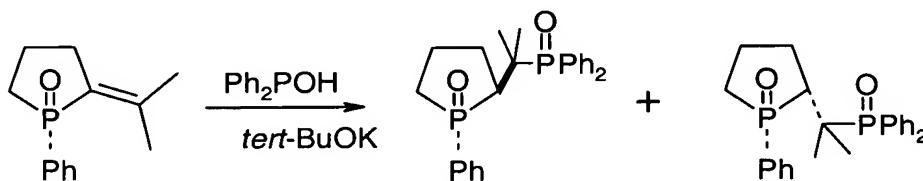
Step 2



[0077] The same procedure as described in Example 2 was employed, but with trans-2-(1-hydroxy-1-methyl-ethyl)-1-phenylphospholane 1-oxide as a substrate, yielded: 36% of trans-2-(1-chloro-1-methyl-ethyl)-1-phenylphospholane 1-oxide as a colorless oil; ¹H NMR (500MHz) δ: 1.68 (s, 3H), 1.69-1.79 (m, 1H), 1.85 (s, 3H), 2.13-2.38 (m, 4H), 2.38-2.52 (m, 2H), 7.47-7.57 (m, 3H), 7.69-7.77 (m, 2H); ¹³C NMR (126MHz) δ: 22.5 (d, *J* = 3.7), 28.8 (d, *J* = 11.4), 30.0 (d, *J* = 1.5), 31.9 (d, *J* = 67.5), 33.0 (d, *J* = 1.9), 55.6 (d, *J* = 62.3), 72.0 (d, *J* = 2.6), 128.8 (d, *J* = 11.7), 130.0 (d, *J* = 9.6), 131.9 (d, *J* = 2.9), 134.1 (d, *J* = 90.9); ³¹P NMR (81MHz) δ: 54.2; EI MS *m/z* (%): 222 (14), 221 (100), 220 (14), 125 (11), 95 (21), 77 (10), 47 (16), 41 (10); LSIMS(+) MS *m/z*: 257 (100, (M + H)⁺), 221 (70); HR LSIMS(+) MS calcd. for C₁₃H₁₉OPCl: 257.0862, found 257.0855; and 51% of 2-isopropylidene-1-phenylphospholane 1-oxide as a colorless oil; ¹H NMR (500MHz) δ: 1.80 (d, *J* = 2.2), 1.83 (d, *J* = 1.6), 1.84-1.93 (m, 1H), 2.02-2.16 (m, 3H), 2.43-2.54 (m, 1H), 2.61-2.73 (m, 1H), 7.39-7.50 (m, 3H), 7.66-7.73 (m, 2H), ¹³C NMR (126MHz) δ: 20.9 (d, *J* = 6.1), 22.9 (d, *J* = 12.5), 23.4 (d, *J* = 8.6), 31.0 (d, *J* = 27.4), 31.1 (d, *J* = 72.2), 128.0 (d, *J* = 98.2), 128.5 (d, *J* = 11.7), 130.4 (d, *J* = 10.3), 131.3 (d, *J* = 2.8), 134.4 (d, *J* = 94.4), 148.5 (d, *J* = 8.4); ³¹P NMR (162MHz) δ: 46.8; EI MS *m/z* (%): 221 (14), 220 (98, M⁺), 219 (100), 205 (18), 192 (21), 191 (12), 143 (11), 125 (20), 77 (13), 67 (10), 47 (28), 41 (12); HR MS calcd. for C₁₃H₁₇OP: 220.1017, found 220.1010.

[0078] Recycling of trans-2-(1-chloro-1-methyl-ethyl)-1-phenylphospholane 1-oxide and its transformation into 2-isopropylidene-1-phenylphospholane 1-oxide using the same procedure as described in Example 2 with DBU increased the total yield of 2-isopropylidene-1-phenylphospholane 1-oxide to yield 67%.

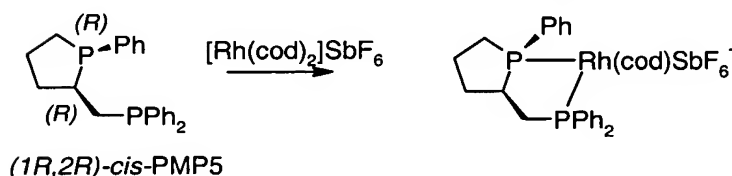
Step 3



[0079] In a 100 mL round bottom 2-neck flask charged with a magnetic stirring bar 140 mg (0.64 mmol) of 2-isopropylidene-1-phenylphospholane 1-oxide and 138 mg (1.5 eq.) of diphenylphosphine oxide were dissolved in 40 mL of dry THF. 110 mg (2 eq.) of potassium *tert*-butoxide was added and the reaction was stirred four hours. Additional 138 mg of diphenylphosphine oxide and 110 mg of *tert*-BuOK were added and the stirring was continued at rt overnight. Next 200 mL of water was added and the mixture was extracted with chloroform (4 x 50 mL). Combined organic phases were dried over MgSO₄, concentrated and purified by chromatography (ethyl acetate : methanol 10:1). Yield: 33% of substrate 2-isopropylidene-1-phenylphospholane 1-oxide, 8 mg (3%) of *trans*-2-(1-diphenylphosphinoyl-1-methyl-ethyl)-1-phenylphospholane 1-oxide as a colorless oil; ¹H NMR (500MHz) δ: 1.26 (d, *J* = 16.6, 3H), 1.35-1.53 (m, 1H), 1.73 (d, *J* = 16.0), 1.81-2.26 (m, 5H), 2.26-2.47 (m, 1H), 7.38-7.55 (m, 10H), 7.55-7.63 (m, 1H), 7.64-7.79 (m, 1H), 7.86-7.97 (m, 3H); ³¹P NMR (162MHz) δ: 37.7 (d, *J* = 47.4), 58.5 (d, *J* = 47.4); EI MS *m/z* (%): 422 (7, M⁺), 222 (15), 221 (100), 55 (13), 53 (11), 51 (30); HR MS calcd. for C₂₅H₂₈O₂P₂: 422.1565, found 422.1561; and 200 mg (64%) of *cis*-2-(1-diphenylphosphinoyl-1-methyl-ethyl)-1-phenylphospholane 1-oxide as white powder; mp 143-146°C (hexane); ¹H NMR (500MHz) δ: 0.68 (d, *J* = 15.3, 3H), 1.13-1.28 (m, 1H), 1.40 (d, *J* = 17.1, 3H), 1.59-1.80 (m, 2H), 1.87-2.09 (m, 3H), 2.38-2.63 (m, 1H), 7.28-7.53 (m, 9H), 7.68-7.82 (m, 4H), 7.95-8.03 (m, 2H); ¹³C NMR (126MHz) δ: 17.3, 21.0 (d, *J* = 3.2), 23.8 (d, *J* = 4.4), 26.8 (d, *J* = 68.9), 27.3 (d, *J* = 14.3), 38.3 (dd, *J* = 1.6, *J* = 67.2), 50.1 (d, *J* = 61.3), 128.1 (d, *J* = 10.9), 128.6 (d, *J* = 11.1), 128.7 (d, *J* = 10.7), 130.3 (d, *J* = 89.1), 131.4 (d, *J* = 2.7), 131.7 (d, *J* = 9.2), 131.9 (d, *J* = 2.53), 132.1 (d, *J* = 7.8), 132.3 (d, *J* = 8.0), 134.7 (d, *J* = 87.7); ³¹P NMR (202MHz) δ: 40.0 (d, *J* = 48.8), 57.4 (d, *J* = 48.8); EI MS *m/z* (%): 422 (7, M⁺), 244 (13), 222 (14), 221 (100), Elemental Anal. Calcd. for C₂₅H₂₈O₂P₂: C 71.08, H 6.68, found C 70.85, H 6.74.

Example 13a

Preparation of [(η -1,2,5,6)-1,5-Cyclooctadiene][(1*R*,2*R*)-*cis*-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate
 $\{[\text{Rh}((R,R)\text{-cis-PMP5})(\text{cod})]\text{SbF}_6\}$



[0080] In a 100 ml round bottom 2-neck flask flushed with argon and equipped with a magnetic stirring bar 166.56 mg $\text{Rh}(\text{cod})_2\text{SbF}_6$ was dissolved in 100 ml dry THF. The mixture was cooled to -80°C and a solution of 108.60 mg (*1R,2R*)-*cis*-1-phenyl-2-[(diphenylphosphino)methyl]phospholane {(*R,R*)-*cis*-PMP5} in 50 ml THF was added dropwise. The mixture was allowed to warm to room temperature, the solvent was evaporated and the residue was dissolved in THF/ CH_2Cl_2 (1:1). A few drops of hexane were added to render the solution turbid, then a few drops of methanol were added. Again a few drops of hexane were added. Overnight an orange-yellow precipitate formed which was filtered and washed with hexane. Yield 194.76 mg (80%) of [(η -1,2,5,6)-1,5-cyclooctadiene][(1*R*,2*R*)-*cis*-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate as an orange solid. ^{31}P NMR (300MHz) δ : 50.6 (dd, $J = 26.7$, $J = 148.5$), 70.8 (dd, $J = 26.7$, $J = 146.3$).

Example 13b

Preparation of [(η -1,2,5,6)-1,5-Cyclooctadiene][(1*S*,2*S*)-*cis*-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate $\{[\text{Rh}((S,S)\text{-cis-PMP5})(\text{cod})]\text{SbF}_6\}$

[0081] The complex [(η -1,2,5,6)-1,5-cyclooctadiene][(1*S*,2*S*)-*cis*-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate was prepared analogously to Example 9a) starting from (*1S,2S*)-*cis*-1-phenyl-2-[(diphenylphosphino)methyl]phospholane {(*S,S*)-*cis*-PMP5}.

Example 13c

Preparation of [(η -1,2,5,6)-1,5-Cyclooctadiene][(1*R*,2*S*)-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate {[Rh((*R*,*S*)-*trans*-PMP5)(cod)]SbF₆}

[0082] The complex [(η -1,2,5,6)-1,5-cyclooctadiene][(1*R*,2*S*)-*trans*-1-phenyl-2-[(diphenylphosphino- κ P)methyl]phospholane- κ P]rhodium(1+) hexafluoroantimonate which was needed for comparison experiments was prepared analogously to Example 9a) starting from (1*R*,2*S*)-*trans*-1-phenyl-2-[(diphenylphosphino)methyl]phospholane {(*R*,*S*)-*trans*-PMP5} red solid, yield 88%; ³¹P NMR (300MHz) δ : 56.5 (dd, *J* = 26.7, *J* = 147.0), 74.8 (dd, *J* = 26.7, *J* = 145.5).

Examples of hydrogenations

[0083] The hydrogenation examples were carried out as follows:

In a dry box, an autoclave with a 20 ml glass tube insert was charged with a magnetic stirring bar, the hydrogenation substrate (1 mmol), anhydrous degassed methanol (7 ml) and the metal complex pre-catalyst (0.81 mg, 0.001mmol).

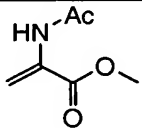
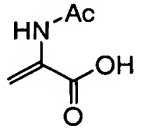
[0084] After 5 cycles of evacuation/filling with hydrogen, the autoclave was pressurized to an initial pressure of 150 kPa. The reaction was stirred at room temperature for 2 h. The reaction mixture was concentrated and the residue was analyzed by GC.

[0085] Preferably, the metal complex pre-catalyst was prepared as described in Example 9 and used in its isolated form for the hydrogenation. Alternatively, the complex may be prepared *in situ*, as described in Example H.

Example A

[0086] Hydrogenation of 2-acetylamino-acrylic acid methyl ester and 2-acetylamino-acrylic acid, respectively, using an isolated pre-catalyst [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 as the Ligand). The hydrogenation was carried out in methanol (MeOH) at room temperature at an initial H₂ pressure as indicated in table A:

Table A

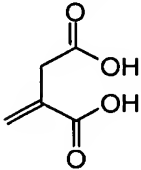
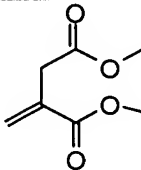
Substrate	Ligand	Initial H ₂ pressure kPa	Time (h)	S/C	% conv. ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	100	94 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	100	33 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	91 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	93 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	100	85 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	100	16 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	82 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	84 (<i>S</i>)

¹⁾Determined by GC [area-%]. ²⁾Determined by GC on a chiral column.

Example B

[0087] The hydrogenation of 2-methylene-succinic acid and 2-methylene-succinic acid dimethyl ester, respectively, with isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 as the Ligand) was carried out in methanol (MeOH) at room temperature at an initial H₂ pressure as indicated in table B:

Table B

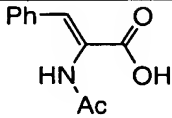
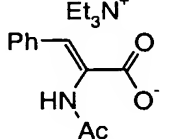
Substrate	Ligand	Initial H ₂ pressure kPa	Time (h)	S/C	% conv. ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	99.8	97 (<i>R</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	100	68 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	96 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	97 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	77	91 (<i>R</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	100	62 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	89 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	90 (<i>R</i>)

¹⁾Determined by GC [area-%]. ²⁾ Determined by GC on a chiral column.

Example C

[0088] The hydrogenation of 2-acetylamino-3-phenyl acrylic acid and 2-acetylamino-3-phenyl acrylic acid triethylammonium salt, respectively, was carried out with 0.1 mol% isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ with *cis*-PMP5 or *trans*-PMP5 as the Ligand in methanol (MeOH) at room temperature at an initial H₂ pressure as indicated in table C:

Table C

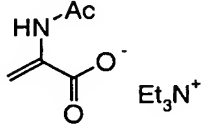
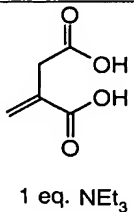
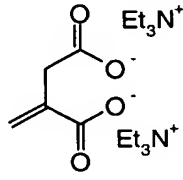
Substrate	Ligand	Initial H ₂ pressure kPa	Time (h)	S/C	% conv. ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	75	98 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	16	1 000	100	98 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	100	25 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	96 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	97 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	16	1 000	78	98 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	16	1 000	100	48 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	1 000	57	98 (<i>S</i>)

¹⁾Determined by GC [area-%] ²⁾ Determined by GC on a chiral column.

Example D

[0089] The hydrogenation of the 2-acetylamino-acrylic acid triethylammonium salt, the 2-methylene-succinic acid and of 2-methylene-succinic acid bis(triethylammonium) salt, respectively, was carried out with 0.1 mol% isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 as the Ligand) in methanol (MeOH) at room temperature at an initial H₂ pressure as indicated in table D:

Table D

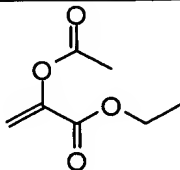
Substrate	Ligand	Initial H ₂ pressure	Time (h)	S/C	% conv. ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	1.5	2	1 000	100	96 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	1.5	2	1 000	99	57 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	5	3	1 000	100	96 (<i>R</i>)
 1 eq. NEt ₃	(<i>R,R</i>)- <i>cis</i> -PMP5	1.5	2	1 000	99.9	98 (<i>R</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	1.5	2	1 000	100	77 (<i>R</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	5	16	1 000	100	96 (<i>R</i>)
 Et ₃ N ⁺	(<i>R,R</i>)- <i>cis</i> -PMP5	1.5	2	1 000	90	96 (<i>R</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	1.5	2	1 000	100	85 (<i>R</i>)

¹⁾Determined by GC [area-%]. ²⁾Determined by GC on a chiral column.

Example E

[0090] The hydrogenation of the 2-acetyloxy-acrylic acid ethyl ester was carried out with 0.1 mol% isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 or Prophos as the Ligand) in methanol (MeOH) at room temperature at an initial H₂ pressure as indicated in table E:

Table E

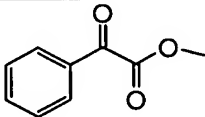
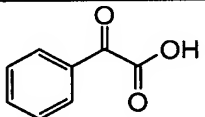
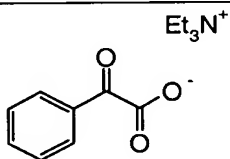
Substrate	Ligand	Initial H ₂ kPa	Time (h)	S/C	% conv. ¹⁾	% ee ²⁾
	(<i>R</i>)-Prophos	500	3	100	100	78 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	2	1 000	33	95 (<i>S</i>)
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	2	1 000	35	23 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	3	100	100	97 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	1 000	100	97 (<i>S</i>)
	(<i>R,R</i>)- <i>cis</i> -PMP5	500	16	10 000	45	97 (<i>S</i>)

¹⁾Determined by GC [area-%], ²⁾Determined by GC on a chiral column.

Example F

[0091] The hydrogenation of the oxo-phenylacetic acid methyl ester, oxo-phenylacetic acid and oxo-phenylacetic acid triethylammmonium salt, respectively, was carried out with 0.1 mol% isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 as the Ligand) in methanol (MeOH) at room temperature at an initial H₂ pressure of 4000 kPa for 4 h. The results are shown in table F:

Table F

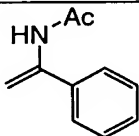
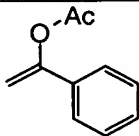
Substrate	Ligand	% conversion ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	8	2
	(<i>R,S</i>)- <i>trans</i> -PMP5	4	3
	(<i>R,R</i>)- <i>cis</i> -PMP5	80	3
	(<i>R,S</i>)- <i>trans</i> -PMP5	3	5
	(<i>R,R</i>)- <i>cis</i> -PMP5	98	9
	(<i>R,S</i>)- <i>trans</i> -PMP5	36	3

¹⁾ Determined by GC [area-%]. ²⁾ Determined by GC on a chiral column.

Example G

[0092] The hydrogenation of N-(1-phenylvinyl)acetamide and acetic acid 1-phenylvinyl ester, respectively, was carried out with isolated pre-catalysts [Rh(Ligand)(cod)] SbF₆ (with *cis*-PMP5 or *trans*-PMP5 as the Ligand) in methanol (MeOH) at room temperature at an initial H₂ pressure as mentioned in table G:

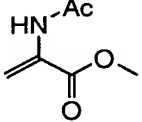
Table G

Substrate	Ligand	Initial H ₂ kPa	Time (h)	S/C	% convers. ¹⁾	% ee ²⁾
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	6	500	100	10
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	6	500	100	20
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	6	500	100	10
	(<i>R,R</i>)- <i>cis</i> -PMP5	150	7	1 000	21	22
	(<i>R,S</i>)- <i>trans</i> -PMP5	150	7	1 000	13	22
	(<i>R,R</i>)- <i>cis</i> -PMP5	1500	7	1 000	78	18

¹⁾Determined by GC [area-%]. ²⁾Determined by GC on a chiral column.

Example H: using a Cationic Catalysts Prepared *in situ*

[0093] In this example the metal complex was prepared *in situ* by dissolving of 0.010 mmol rhodium precursor (Rh(cod)₂X) and 0.011 mmol ligand in 4 ml of methanol. The orange solution was stirred 45 minutes and then mixed with a solution of 1 mmol of substrate dissolved in 3 ml of methanol. Procedure of hydrogenation was carried out as described above catalytic hydrogenation of 2-acetyl-amino-acrylic acid methyl ester was carried out at room temperature with an initial H₂ pressure of 500 kPa, 3h, S/C 100. The ligands X were

Substrate	Ligand	X	Solvent	% conv. ¹⁾	% ee ²⁾
	(<i>S,S</i>)- <i>cis</i> -PMP5	BARF	MeOH	100	81 (<i>R</i>)
	(<i>S,S</i>)- <i>cis</i> -PMP5	PF ₆	MeOH	100	82 (<i>R</i>)
	(<i>S,R</i>)- <i>trans</i> -PMP5	PF ₆	MeOH	100	5 (<i>R</i>)

¹⁾Determined by GC [area-%]. ²⁾Determined by GC on a chiral column.